



Pain In Women

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Women (or those assigned female at birth) are more likely to experience almost all forms of chronic pain than men. Additionally, female anatomy and physiology are associated with forms of pain unique to women and can lead to specific challenges. Failure to consider these conditions and challenges contributes to the burden of pain for women throughout their lives.*

Painful conditions uniquely affecting women

Dysmenorrhoea

The onset of periods (menarche) is usually the first experience of pain related to female anatomy/physiology (although ovarian cysts and vulvar pain can occur in younger children too). Painful periods (dysmenorrhoea) are incredibly common with up to 90% of adolescents and young women describing some form of pain with their period and 30-40% experiencing pain severe enough to impact on school/work attendance. Although frequently dismissed as a normal part of being a woman, we are increasingly aware of the wider impact of period pain on academic achievement, mental health, social development, and life course potential^[1]. Period pain can be associated with another disease (secondary) or occur in the absence of an identifiable cause (primary). There is no clear way to discern this difference from the patient's medical history, and thus it is important to take the report of period pain seriously and treat it promptly to reduce its interference with the quality of life^[2], whether or not further investigation is being undertaken.

Common pathologies associated with secondary dysmenorrhoea are endometriosis and adenomyosis. Endometriosis occurs in

approximately 1 out of 10 women and is characterized by the presence of tissue that resembles the womb lining (endometrium) outside of the womb^[3]. Adenomyosis is a related condition where the tissue resembling the womb lining is found in the muscle layer of the womb. The two conditions frequently co-exist, and it is likely that there are common factors underlying their development. Until recently, the diagnosis of adenomyosis could only be made after hysterectomy (removal of the womb surgically) and therefore our understanding of the disease and its associated symptoms, particularly in younger women, is relatively limited. However, it is likely that adenomyosis explains much of the heavy bleeding seen in association with period pain^[4].

Endometriosis is commonly associated with other types of pelvic pain, including non-cyclical pain, pain with sex (dyspareunia), pain with bowel opening (dyschezia), and pain with bladder emptying (dysuria). However, it is well established that the pain symptoms described by those with endometriosis do not necessarily relate to either the location or severity of the disease (i.e., those with mild disease can have disabling pain and those with severe disease may have minimal pain). Importantly, many women with endometriosis have no pain symptoms at all, and their disease may be found in association with subfertility or incidentally during a scan or a surgical procedure for another reason than endometriosis. In addition to pelvic pain, many women describe other symptoms such as fatigue and poor mental health (depression and anxiety); other pain conditions (e.g. fibromyalgia, irritable bowel syndrome, migraine) and auto-immune/inflammatory diseases (e.g. asthma, rheumatoid arthritis) commonly co-exist.

* Throughout this factsheet we use gendered terminology for clarity however the issues raised are relevant for any person born with female anatomy.

This complex and varied presentation, in combination with the lack of a non-invasive diagnostic test, contributes to the well-established diagnostic delay for those with endometriosis (7–11 years across the developed world) and means that those with endometriosis-associated pain will meet the definition of chronic pain (pain for >3 months) long before they gain a diagnosis. Importantly it has also led to the reconceptualization of endometriosis as a systemic disease (involving the whole person rather than just the pelvis) and the description of an endometriosis syndrome, diagnosed only when a patient has both visible lesions and symptoms [5].

Hormone therapies that stop or reduce periods (e.g., contraceptive pills, high dose progestogens, progestogen-releasing coils (intrauterine systems), “menopause injections” (GnRH analogues) are often useful for treating dysmenorrhoea, but the symptoms almost always return upon cessation of the therapy. These therapies are also recommended for endometriosis and adenomyosis as they suppress the ectopic tissue.

Surgery is another treatment option. For adenomyosis, the only surgical approach is a hysterectomy, which is not an appropriate option for younger women. For endometriosis, the ectopic tissue can either be excised or burnt away. Unfortunately, approximately 50% women will still have pain after surgical and/or hormonal treatment. Despite an increasing awareness that a more multi-disciplinary approach to the management of endometriosis-associated pain is needed (as used for other forms of chronic pain), there is relatively little clinical trial data supporting these approaches and they remain unavailable to many women [3,5]. Even where they are available, they are likely to be offered late in the patient journey.

Vulvodynia

The area at the entrance to the vagina that includes the clitoris, urethra and labia minora and majora is known as the vulva. Pain in the vulval area is common, yet studies suggest that only 60% of women who report chronic vulvar pain seek treatment and approximately half of those women never receive a diagnosis [6]. Vulvar pain can be caused by specific disorders (including infections, inflammatory diseases, neoplasia, neurologic causes, trauma, hormonal deficiencies), in which case treatment is directed towards the underlying cause, or it can be idiopathic (i.e., without an identified cause) [7,8]. Pain in the vulvar area without an identifiable cause has been termed vulvodynia or primary vulval pain syndrome and can occur spontaneously or with touch situations (e.g., during sexual activity, prolonged sitting, tampon insertion) [7,9]. Vulvodynia/vulval pain syndrome can be further subdivided into localized vs. generalized depending on where pain is experienced [7,8]. It is estimated that

between 13–16% of women will experience vulvodynia, and while it is most common in younger women, it can also persist or develop into postmenopause [6,7]. Vulvodynia is associated with a reduced quality of life and reduced sexual satisfaction in women and their partners and often presents a significant economic burden [10].

Vulvodynia has a multi-factorial etiology ranging from biological to psychosocial factors (summarized in [7]). Vulvodynia is a diagnosis of exclusion (ruling out the specific disorders listed above) and can be summarized as sensitivity at the vaginal opening on cotton-swab testing, in association with normal vulvar appearance (with or without local erythema) and normal vaginal walls and secretions [7]. Multiple treatment options have been suggested for vulvodynia, including pelvic floor physical therapy, psychological interventions, pharmacological therapy, or a combination of the above [7]. Benefit from vestibulectomy (surgical removal of the vulvar vestibule) has been reported in selected cases with refractory vulvodynia [11]; however current recommendations are that this should only be offered to those who do not respond to all other options.

Mastalgia

Breast pain (mastalgia) is common in women and also in male-to-female transgender people after hormonal treatment. There is a distinction between cyclic and noncyclic breast pain; whereas cyclic breast pain typically starts days (up to a week) before the menstrual period starts, non-cyclic breast pain occurs throughout the month unrelated to the menstrual cycle.

Cyclic breast pain typically occurs in menstruating females, females using hormone treatment, or during menopause. It usually affects both breasts and is often described as dull or aching. Although it is mainly benign, it is still difficult to treat.

Non-cyclic breast pain can relate to very different causes. Typically, only one breast is affected, and it typically occurs after menopause, for example by trauma, due to breast surgery, or diseases unrelated to the breast (like chest wall or muscle pain) [12]. New onset breast pain, especially when unilateral, may be associated with malignancy and thus should always prompt investigation.

Pregnancy pain

Breast pain is also common in early and late pregnancy, the post-natal period, and throughout the lactation period. In the majority of individuals, breast pain occurs in response to hormonally driven changes to breast tissue, engorgement with milk, or nipple trauma. However, it can also signal mastitis, and thus other features of infection (e.g., fever or systemic symptoms) should be investigated.

The anatomical changes of pregnancy are associated with a variety of other pains, particularly in the pelvis, hips and lower back. Pregnancy complications, both early (miscarriage, ectopic pregnancy) and late (placental abruption, uterine rupture, preterm labour) are also commonly associated with pain. Antenatal care/education thus highlights the need to pay attention to and act on pain, perhaps in contrast to the message usually given to women that pain is to be tolerated, if not expected. Unfortunately, the physical burden of pregnancy can be slow to resolve, and many women, particularly those who continue to breastfeed, describe persistent pelvic girdle pain long after birth, since high levels of progesterone promote muscle laxity^[13].

Specific challenges associated with pain in women

Although the experience of pain is in many ways similar across sexes and genders, there are some specific challenges for women. Pelvic pain is a huge problem, accounting for approximately 20% of gynaecological consultations as well as many with other secondary care specialists and primary care physicians^[14]. Pelvic pain is frequently visceral in origin, which is diffuse in character and typically presents as a dull sensation that cannot be clearly related to an organ. It can be associated with autonomic reactions, such as nausea, vomiting, sweating, and increases or decreases in blood pressure^[15]. Visceral pain is often referred to non-visceral tissues. For example, women with dysmenorrhea often experience low back pain and pain radiating to the legs.

There is increasing recognition that chronic pelvic and urogenital pain conditions rarely occur alone, but are often accompanied by other chronic pain conditions, which can be inside or outside of the pelvic area. The concept of these Chronic Overlapping Pain Conditions (COPCs) has been recognized by the US National Institutes of Health and the United States Congress^[16]. COPCs predominantly affect women resulting in a significantly higher pain burden and increasing the negative effect of pain on women's lives^[17]. They also have important clinical implications. Women with COPCs are typically seen by healthcare providers in different medical subspecialties for each pain condition. Rather than such a fragmented approach, a concerted effort to address the overlapping aspects of the different pain complaints will be imperative to treat the whole patient. In support of this approach, recent clinical observational studies have shown that, in women with COPCs, treatment of one pain syndrome may result in improvement of another COPC as well^[18].

Whilst pain has a well-established impact on quality of life, it is important to remember that many of the painful conditions that most commonly affect women will have other life-impacting symptoms as well. For example, endometriosis is commonly associated with in-

fertility; adenomyosis and dysmenorrhoea with heavy vaginal bleeding; and other pelvic pain conditions/syndromes with incontinence (of both urine and stool) or with urinary urgency, diarrhea, or constipation. Management approaches that do not also take into account these symptoms (which may not track with pain^[19]) are unlikely to markedly improve quality of life. Additionally, many female-specific pains are intimate in nature, associated with functions/processes that have societal or cultural taboos, myths, and misinformation. Sensitivity to these nuances, making time to enquire about the patient's understanding, and providing appropriate education where needed can only enhance the therapeutic relationship.

One major problem in pain research in general, and research related to pain in female-specific diseases in particular, is outcome assessment. Chronic pain is inherently a bio-psycho-social disease. However, in most pain-related studies, pain intensity is the primary (and in many studies the only) outcome measured, whereas other domains, e.g., those related to psycho-social aspects, are much less considered. A recent study has shown that, for endometriosis-related pain trials, outcome assessment is quite variable^[20]; this is in line with other reviews of pelvic pain conditions^[21].

This lack of consistency has led to three major problems. First, the outcomes are often not related to what patients with the condition (and professionals focusing on pain treatment) consider as important. Second, if different outcomes and outcome assessment tools are chosen, results from trials are difficult to compare, hindering evidence-based conclusions and treatment recommendations. Finally, the outcome measures used in trials to assess endometriosis-specific pain-related symptoms often lack proper development processes. Thus, there is an urgent need to define the most relevant outcomes that should be assessed in clinical trials related to pain in female-specific diseases and to develop better outcome measures.

Approaches to management of pain in women

Female-specific forms of chronic pain interfere with many areas of life, and thus holistic, multi-disciplinary management approaches, such as those recommended for other chronic pain conditions, are likely to be required for optimum benefit. As with any form of chronic pain, it is important to identify and treat any relevant underlying pathology before taking a pain-management approach. However, the visceral origin and diagnostic challenges associated with many female-specific pains mean that the search for an underlying cause can be time-consuming; it is important to ensure adequate analgesia is provided during this time, although opiates should be avoided when possible.

Pain occurs throughout life for women, and treatment strategies must take lifestage into consideration. For example, hormonal therapies or potentially teratogenic medication will not be appropriate for those trying to conceive or during pregnancy, while intensive in-person pain management courses may not be feasible for a woman who is already trying to juggle work and a young family. Pain during pregnancy requires a different focus to ensure the health of both mother and baby. On the other hand, it is important to remember that acute pain on the background of chronic pain may represent a different pathology (e.g., ovarian torsion, appendicitis, malignancy) with potentially serious consequences. Thus, clinical expertise is required to determine the extent to which new investigations should be arranged.

Recent work has highlighted the importance of pain education for women with chronic pelvic pain and how rarely this is included in clinical guidance^[22]. Widespread adoption of pain education early in the care of women with persistent pain is essential to reduce the burden of pain on both women and healthcare services. Sadly, traumatic experiences are common in the population as a whole and women are over-represented in those affected, particularly in terms of sexual assault/abuse and intimate partner violence. Therefore, all care should be delivered with a trauma-informed approach^[14].

Conclusion

The burden of pain for women is significant throughout their lives. Whilst general approaches to pain may be appropriate, there are many reasons why a sex-specific approach can often be required. Education is key to reducing the pain burden. This includes education of clinicians and researchers on sex-specific factors and pain education as a component of pain management approaches. Perhaps most importantly, education must take place at a societal level to dispel taboos and misinformation around women's health; only then will it be no longer considered normal—and thus acceptable—for women to suffer pain.

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